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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	PAPER NUMBER
1634	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/684,346	CHUN ET AL.	
	Examiner	Art Unit	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,58-61,82-91,106-108,117,131-135,157-159,228,229,231,232 and 234-237* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/13/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-9,58-61,82-91,106-108,117,131-135,157-159,228,229,231,232 and 234-237.

DETAILED ACTION

1. This action is in response to papers filed 9/13/2010

2. Currently, Claims 1-9, 58-61, 82-91, 106-108, 117, 131-135, 157-159, 228-229, 231-232, and 234-237 are pending. Claims 10-57, 62-81, 92-105, 109-116, 118-132, 136-156, 160-227, 230, and 233 have been cancelled.

3. The rejections presented in the previous office action are maintained but have been amended to address the new amendments and new claims. Response to arguments follows the rejection.

4. This action is Final.

Withdrawn Rejections

5. The rejection of Claims 58-61 under 35 USC 112/2nd made in sections 8 of the previous office action are moot based upon amendments to the claims which correct the insufficient antecedent basis for the limitation “said second hybridized duplex”.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on 9/13/2009 has been considered by the examiner.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 4-5, 7-9, 58, 60, 90-91, 228, 231-232, 234-237 are rejected under 35 U.S.C. 102(b) as being anticipated by Lannigan et al. (US Patent 6399302 June 4, 2002).

This rejection has been maintained by has been modified to encompass the new limitations of the claims and the newly recited Claims 236-237.

With regard to Claim 1, Lannigan et al. teaches a probe (e.g. an oligonucleotide) (column 8 lines 13-15). Lannigan et al. teaches that the oligonucleotides comprise the format F1-X-A-L-B-Y-F2 (column 8 lines 17). With regard to Claim 1a, Lannigan et al. teaches the probe comprises X and Y. Lannigan et al teaches that X and Y are short complementary oligonucleotide sequences that are about 3 to about 15 nucleotides in length (column 8 lines 20-30). As such X and Y would represent a first object sequence and a first complement sequence that are about 3 to about 15 nucleotides and are substantially complementary to each other and are hybridized (column 8 lines 30-35).

With regard to claim 1b, Lannigan et al. teaches A and B. Lannigan et al. teaches that A and B represent aptamers that bind to a target analyte (column 8 lines 21-23). As such Lannigan et al. teach a recognition element conjugated to the first

object or the first complement sequences (e.g. A or B would be considered recognition elements).

The claims are drawn to a structure wherein a recognition element is conjugated to at least one of said first object and first complement sequences through a coupling element. Lannigan teaches that L connects (conjugates) A (recognition element) to Y (complement sequence). Lannigan et al. teaches that the linker (e.g. coupling element) is about 50 or more bases (column 6 lines 60-65). Lannigan et al. teaches that A and B can range from 10 to about 100 bases (column 6 lines 58-60). Therefore the target, since both A and B hybridize to different parts of the structure is at least 10 to about 100 bases. Therefore the coupling element would be the same size or shorter than the size of the target agent wherein the target agent is 51 to 100 bases.

With regard to Claim 1c, Lannigan et al. teaches the probe comprises F1 and F2. Lannigan et al. teaches that F1 and F2 represent a signaling system such as FRET (column 8 line 19 and lines 1-3). Lannigan et al. teaches that this detectable label produces a signal whose level is a function of the amount of probe (Column 10 lines 10-30).

With regard to the wherein statement of "recognition element is conjugated through said coupling element to a location inside the first hybridized duplex region of said first object or first complement sequence so that the recognition element is branched out from said first hybridized duplex", Lannigan et al. does not specifically use the descriptor of "branched out". However, Lannigan et al. teaches that A and B (recognition elements) are located between the first object and first complement.

Therefore when the first object and first complement are hybridized together, the recognition elements would stick out from the duplex (e.g. branch out).

Lannigan et al. teaches that in the presence of the target, the recognition elements bind to the target and therefore force the duplex to separate (e.g. alters the amount of the first hybridized duplex) (Column 8 lines 30-35). Lannigan et al. teaches that upon the interaction of the target agent to the recognition element, the signal is altered (column 8 lines 35-40).

With regard to Claim 4, Lannigan et al. teaches that the object and complement sequences are comprised of DNA or RNA (column 8 lines 27-28).

With regard to Claim 5, Lannigan et al. teaches a probe (e.g. an oligonucleotide) (column 8 lines 13-15). Lannigan et al. teaches that the oligonucleotides comprise the format F1-X-A-L-B-Y-F2 (column 8 lines 17). With regard to Claim 5a, Lannigan et al. teaches the probe comprises X and Y. Lannigan et al teaches that X and Y are short complementary oligonucleotide sequences that are about 3 to about 15 nucleotides in length (column 8 lines 20-30). As such X and Y would represent a first object sequence and a first complement sequence that are about 3 to about 15 nucleotides and are substantially complementary to each other and are hybridized (column 8 lines 30-35).

With regard to claim 5b, Lannigan et al. teaches A and B. Lannigan et al. teaches that A and B represent aptamers that bind to a target analyte (e.g. aptamers represent ligands) (column 8 lines 21-23). As such Lannigan et al. teach a ligand conjugated to the first object and first complement sequences.

The claims are drawn to a structure wherein a ligand is conjugated to at least one of said first object and first complement sequences through a coupling element. Lannigan teaches that L connects (conjugates) A (ligand) to Y (complement sequence). Lannigan et al. teaches that the linker (L) (e.g. coupling element) is 0 to about 50 or more bases (column 6 lines 60-65). Lannigan et al. teaches that A and B can range from 10 to about 100 bases (column 6 lines 58-60). Therefore the target, since both A and B hybridize to different parts of the structure is at least 10 to about 100 bases. Therefore the coupling element would be the same size or shorter than the size of the target wherein the target is about 100 bases. This target would be considered a receptor agent, as it is molecular entity which specifically binds to a complementary molecular entity (see definition of receptor agent in instant specification paragraph174).

With regard to Claim 5c, Lannigan et al. teaches the probe comprises F1 and F2. Lannigan et al. teaches that F1 and F2 represent a signaling system such as FRET (column 8 line 19 and lines 1-3). Lannigan et al. teaches that this detectable label produces a signal whose level is a function of the amount of probe (Column 10 lines 10-30).

With regard to the wherein statement of "ligand is conjugated through said coupling element to a location inside the first hybridized duplex region of said firth object or first complement sequence so that the ligand is branched out from said first hybridized duplex", Lannigan et al. does not specifically use the descriptor of "branched out". However, Lannigan et al. teaches that A and B (ligands) are located between the first object and first complement. Therefore when the first object and first complement

are hybridized together, the recognition elements would stick out from the duplex (e.g. branch out).

Lannigan et al. teaches that in the presence of the target, the ligand bind to the target and therefore force the duplex to separate (e.g. alters the amount of the first hybridized duplex) (Column 8 lines 30-35). Lannigan et al. teaches that upon the interaction of the receptor agent to the ligand, the signal is altered (column 8 lines 35-40).

With regard to Claims 7-8, Lannigan et al. teaches that the coupling elements are linked using covalently bonds such as chemical bonds (column 6 lines 5-15).

With regard to Claim 9, Lannigan et al. teach that the ligand is nucleic acids (column 1 lines 50-55).

With regard to Claims 58 and 60, Lannigan et al. teaches that in the absence of the target agent (e.g. the target) the probe forms a hairpin structure and therefore a first hybridized duplex is preferentially formed, however, in the presence of the target agent (e.g. excess) the probe hybridizes to the target agent (column 2 lines 50-60).

With regard to claim 90, Lannigan et al. teaches an interactive label pair comprising a first label moiety conjugated to a first object sequence and a second label moiety conjugated to a first complement sequence, wherein the moieties interact with the first hybridization duplex is formed (column 3 lines 45-60).

With regard to Claim 91, Lannigan et al. teaches a probe with an interactive fluorescer and quencher wherein the interaction causes a change in wavelength (column 3 lines 45-60 and column 4 lines 5-10).

With regard to Claim 228, Lannigan et al. teaches that multiple probes can be made (e.g. a target detection system) (column 2 lines 45-50).

With regard to Claims 232 and 235, Lannigan et al. teaches that the linker (L) (e.g. coupling element) is 0 to about 50 or more bases (column 6 lines 60-65). As such the coupling agent is less than 100 nm in length.

With regard to Claims 231 and 234, Lannigan et al. teaches that A and B can range from 10 to about 100 bases (column 6 lines 58-60). Therefore the target, since both A and B hybridize to different parts of the structure is at least 20 to about 200 bases. As such the receptor agent or target agent has a size of between 1 nm and 100nm.

With regard to Claim 236, Lannigan et al. teaches a probe (e.g. an oligonucleotide) (column 8 lines 13-15). Lannigan et al. teaches that the oligonucleotides comprise the format F1-X-A-L-B-Y-F2 (column 8 lines 17). With regard to Claim 236a, Lannigan et al. teaches the probe comprises X and Y. Lannigan et al teaches that X and Y are short complementary oligonucleotide sequences that are about 3 to about 15 nucleotides in length (column 8 lines 20-30). As such X and Y would represent a first object sequence and a first complement sequence that are about 3 to about 15 nucleotides and are substantially complementary to each other and are hybridized (column 8 lines 30-35).

With regard to claim 236b, Lannigan et al. teaches A and B. Lannigan et al. teaches that A and B represent aptamers that bind to a target analyte (column 8 lines 21-23). As such Lannigan et al. teach at least one recognition element conjugated to

the first object or the first complement sequences (e.g. A or B would be considered recognition elements).

The claims are drawn to a structure wherein a recognition element is conjugated to at least one of said first object and first complement sequences through a coupling element. Lannigan teaches that L connects (conjugates) A (recognition element) to Y (complement sequence). Lannigan et al. teaches that the linker (e.g. coupling element) is about 50 or more bases (column 6 lines 60-65). Lannigan et al. teaches that A and B can range from 10 to about 100 bases (column 6 lines 58-60). Therefore the target, since both A and B hybridize to different parts of the structure is at least 10 to about 100 bases. Therefore the coupling element would be the same size or shorter than the size of the target agent wherein the target agent is 51 to 100 bases.

With regard to Claim 236c, Lannigan et al. teaches the probe comprises F1 and F2. Lannigan et al. teaches that F1 and F2 represent a signaling system such as FRET (column 8 line 19 and lines 1-3). Lannigan et al. teaches that this detectable label produces a signal whose level is a function of the amount of probe (Column 10 lines 10-30).

Lannigan et al. teaches that in the presence of the target, the recognition elements bind to the target and therefore force the duplex to separate (e.g. alters the amount of the first hybridized duplex) (Column 8 lines 30-35). Lannigan et al. teaches that upon the interaction of the target agent to the recognition element, the signal is altered (column 8 lines 35-40).

With regard to the wherein statement "wherein said recognition element is conjugated through said coupling element to a location at least one nucleotide inside the first hybridized duplex region of said first object or first complement sequence so that the recognition element is branched out form said first hybridized duplex", Lannigan et al. does not specifically use the descriptor of "branched out". However, Lannigan et al. teaches that A and B (recognition elements) are located between the first object and first complement. Therefore when the first object and first complement are hybridized together, the recognition elements would stick out from the duplex (e.g. branch out). Lannigan et al. teaches that the signal generating ligand (e.g. the recognition elements) is attached to the end of the oligonucleotide sequence as such the probe of Lannigan teaches a recognition element is attached (conjugated) through a coupling element and is attached to the end of the first complement sequence (column 8 lines 14-15). This end of the first complement sequence is considered "at least one nucleotide inside the first hybridized duplex" as when the first object and the first complement bind the nucleotide on the 3' end would be considered inside the first hybridized duplex. The term "at least one nucleotide inside" is being interpreted as requiring that the ligand is attached to a nucleotide within the hybridized region.

With regard to Claim 237, Lannigan et al. teaches a probe (e.g. an oligonucleotide) (column 8 lines 13-15). Lannigan et al. teaches that the oligonucleotides comprise the format F1-X-A-L-B-Y-F2 (column 8 lines 17). With regard to Claim 237a, Lannigan et al. teaches the probe comprises X and Y. Lannigan et al teaches that X and Y are short complementary oligonucleotide sequences that are

about 3 to about 15 nucleotides in length (column 8 lines 20-30). As such X and Y would represent a first object sequence and a first complement sequence that are about 3 to about 15 nucleotides and are substantially complementary to each other and are hybridized (column 8 lines 30-35).

With regard to claim 237b, Lannigan et al. teaches A and B. Lannigan et al. teaches that A and B represent aptamers that bind to a target analyte (e.g. aptamers represent ligands) (column 8 lines 21-23). As such Lannigan et al. teach a ligand conjugated to the first object and first complement sequences.

The claims are drawn to a structure wherein a ligand is conjugated to at least one of said first object and first complement sequences through a coupling element. Lannigan teaches that L connects (conjugates) A (ligand) to Y (complement sequence). Lannigan et al. teaches that the linker (L) (e.g. coupling element) is 0 to about 50 or more bases (column 6 lines 60-65). Lannigan et al. teaches that A and B can range from 10 to about 100 bases (column 6 lines 58-60). Therefore the target, since both A and B hybridize to different parts of the structure is at least 10 to about 100 bases. Therefore the coupling element would be the same size or shorter than the size of the target wherein the target is about 100 bases. This target would be considered a receptor agent, as it is molecular entity which specifically binds to a complementary molecular entity (see definition of receptor agent in instant specification paragraph174).

With regard to Claim 237c, Lannigan et al. teaches the probe comprises F1 and F2. Lannigan et al. teaches that F1 and F2 represent a signaling system such as FRET (column 8 line 19 and lines 1-3). Lannigan et al. teaches that this detectable label

produces a signal whose level is a function of the amount of probe (Column 10 lines 10-30).

Lannigan et al. teaches that in the presence of the target, the ligand bind to the target and therefore force the duplex to separate (e.g. alters the amount of the first hybridized duplex) (Column 8 lines 30-35). Lannigan et al. teaches that upon the interaction of the receptor agent to the ligand, the signal is altered (column 8 lines 35-40).

With regard to the wherein statement "wherein said probe ligand is conjugated through said coupling element to a location at least one nucleotide inside the first hybridized duplex region of said first object or first complement sequence so that the probe ligand is branched out form said first hybridized duplex", Lannigan et al. does not specifically use the descriptor of "branched out". However, Lannigan et al. teaches that A and B (probe ligands) are located between the first object and first complement. Therefore when the first object and first complement are hybridized together, the recognition elements would stick out from the duplex (e.g. branch out). Lannigan et al. teaches that the signal generating ligand (e.g. the probe ligands) are attached to the end of the oligonucleotide sequence as such the probe of Lannigan teaches a probe ligand is attached (conjugated) through an coupling element and is attached to the end of the first complement sequence (column 8 lines 14-15). This end of the first complement sequence is considered "at least one nucleotide inside the first hybridized duplex" as when the first object and the first complement bind the nucleotide on the 3' end would be considered inside the first hybridized duplex. The term "at least one nucleotide

inside" is being interpreted as requiring that the ligand is attached to a nucleotide within the hybridized region.

Response to Arguments

The reply traverses the rejection. A summary of the arguments presented in the reply is provided below with response to arguments following.

The reply asserts that the claimed probe features a single recognition element instead of the previous claim encompassing "at least one recognition element" (p. 15 5th-6th paragraph). The reply asserts that therefore the probe of Lannigan does not overcome the cited claims because Lannigan et al. teaches multiple recognition elements (p 15 5th -6th paragraphs).

The reply asserts that Lannigan et al. does not teach a probe conjugated through a coupling element at least one nucleotide inside a first hybridized duplex region of a first object or first complement sequence (p. 17 last paragraph to p. 18 1st paragraph).

These arguments have been fully reviewed but have not been found persuasive.

The reply appears to be asserting that the claimed probe is different from the teaching of the probe of Lannigan et al. because it no longer requires at least one recognition element, but rather "a recognition element". Is noted that structures required by the probe are claimed in the open language of "comprising". Hence, although the claims might require one recognition element, the probe itself can comprise any number of recognition elements. Because of the openness of the claim language this rejection is maintained.

With regard to Claims 236-237, the reply appears to be asserting that the claim language “at least one nucleotide inside a first hybridized duplex region" limits the claims to the attachment conjugated to a nucleotide which is not the first nucleotide at either the 3’ or 5’ end. However, the specification does not define or limit this phrase as such. The phrase is broadly interpreted by the examiner as requiring an attachment to any nucleotide in a region which forms a duplex and it is not limited to any particular nucleotides of the duplex. Herein in the case of Lannigan, he teaches that that the components are attached to the end of each other (column 8 lines 13-16). As such this teaching encompasses the nucleotide at the end of the oligonucleotide sequence which is part of the hybrid formed by Lannigan et al. (Columns 8 lines 30-35). As such Lannigan et al. teaches the newly recited limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. The following rejection is maintained.

Claims 2-3,106-108,117, 131-135,157-159 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lannigan et al. (US Patent 6399302 June 4, 2002) in view of Jayasena et al. (US Patent Application 2001/0055773 December 27, 2001).

Lannigan et al. was cited on IDS 10/27/2008.

Lannigan et al. teaches the structure of the independent claim 1 as discussed in the 35 USC 102 rejection above.

However Lannigan et al. does not teach a probe comprising a second pair of nucleic acid sequences comprising an object and complement region.

With regard to Claim 2, Jayasena et al. teach a structure in which multiple molecular beacons (e.g. probes which are end labeled and have an object and complementary region) can be joined together (Figure 11 and 13). Jayasena et al. teaches that in this probe there are multiple beacons labeled at the end of each object and complementary region (e.g. labeled at the end of the stems) (p. 10 paragraph 99). Jayasena et al. teaches that these multiple beacons give an increased signal relative to singly labeled probes (p. 10 paragraph 99).

With regard to Claim 3, Jayasena et al. teaches that multiple molecular beacons (e.g. probes with first object and second object regions) can be placed together.

Lannigan et al. teaches that the recognition element is placed after the first object and therefore teaches Therefore teaches coupling without the overlapped region of the second objection region being in contact with the recognition element.

With regard to Claims 106-108, the claims are towards linking the first object and first complementary region to pairs of arm sequences that form duplexes, wherein these pairs have labels. Jayasena et al. teach a structure in which multiple molecular beacons (e.g. probes which are end labeled and have an object and complementary region) can be joined together (Figure 11 and 13). Jayasena et al. teaches that in this probe there are multiple beacons labeled at the end of each object and complementary region (e.g. labeled at the end of the stems) (p. 10 paragraph 99). As such Jayasena et al. teaches a probe structure that encompasses the claimed structure such that the arms of molecular beacons are linked to the first object and first complementary region to pairs of arm sequences that form duplexes. These arms sequences each hybridize to one anther when the target is not present. Further, Jayasena et al. teaches at least three of these arm structures linked together (see Figure 11 and 13).

With regard to Claim 117, Lannigan et al. teaches a detectable label consisting of fluoresces and luminescers (column 8 lines 60-65).

With regard to Claim 131, both Lannigan et al. and Jayasena et al. teach that the interactive label pairs are attached at each object sequence and complement sequence (Lannigan et al. Column 8 lines 60-65 and Jayasena p. 8 paragraph 73).

With regard to Claims 132, Lannigan et al. teaches that in the absence of the receptor agent (e.g. the target) the probe forms a hairpin structure and therefore a first

hybridized duplex is preferentially formed, however, in the presence of the receptor agent the probe hybridizes to the target (receptor agent) (e.g. second hybridized duplex (column 2 lines 50-60).

With regard to Claims 133, Lannigan et al. teaches that in the absence of the receptor agent (e.g. the target) the probe forms a hairpin structure and therefore a first hybridized duplex is preferentially formed, however, in the presence of the receptor agent the probe hybridizes to the target (receptor agent) (e.g. second hybridized duplex (column 2 lines 50-60). Jayasena et al. teach a structure in which multiple molecular beacons (e.g. probes which are end labeled and have an object and complementary region) can be joined together (Figure 11 and 13). Jayasena et al. teaches that in this probe there are multiple beacons labeled at the end of each object and complementary region (e.g. labeled at the end of the stems) (p. 10 paragraph 99). As such Jayasena et al. teaches a third and fourth label moiety interacting and a second hybridized duplex forming when the second molecular beacon hybridizing to the target.

With regard to Claims 134-135, Jayasena et al. teaches that the label moieties of the first and third label can be the same and that the interactive pair is a fluorescer and a sequence which causes moieties in wavelength (p. 10 paragraphs 99-100).

With regard to Claims 157-159, the claims are towards linking the first object and first complementary region to pairs of arm sequences that form duplexes, wherein these pairs have labels. Jayasena et al. teach a structure in which multiple molecular beacons (e.g. probes which are end labeled and have an object and complementary region) can be joined together (Figure 11 and 13). Jayasena et al. teaches that in this

probe there are multiple beacons labeled at the end of each object and complementary region (e.g. labeled at the end of the stems) (p. 10 paragraph 99). As such Jayasena et al. teaches a probe structure that encompasses the claimed structure such that the arms of molecular beacons are linked to the first object and first complementary region to pairs of arm sequences that form duplexes. These arms sequences each hybridize to one anther when the target is not present. Further, Jayasena et al. teaches at least three of these arm structures linked together (see Figure 11 and 13).

Therefore it would be prima facie obvious to one of ordinary skill in the art to modify the probe structure of Lannigan et al. to include multiple regions of objection and complementary regions with detectable moieties as taught by Jayasena et al. The ordinary artisan would be motivated to modify the probe structure of Lannigan et al. to include multiple regions of objection and complementary regions with detectable moieties as taught by Jayasena et al. because Jayasena et al. teaches that these multiple beacons give an increased signal relative to singly labeled probes (p. 10 paragraph 99). Therefore the ordinary artisan would have a reasonable expectation of modifying the probe structure to the multiple label structure of Jayasena et al. in order to increase signal and therefore increase detection of the targets.

Response to Arguments

The reply traverses the rejection. A summary of the arguments presented in the reply is provided below with response to arguments following.

The reply asserts that the teachings of Jayasena et al. do not cure the deficiencies of Lannigan with regard to the teaching of a single recognition element (p.

16 2nd paragraph). The reply further asserts that there is no suggestion or teaching in Jayasena to make and use a probe taken individually or together with Lannigan (p. 16 2nd paragraph).

This argument has been fully reviewed but has not been found persuasive.

As noted in the 35 USC 102 rejection and arguments presented above, the claimed probe is claimed with open claim language and as such even though there is a recitation of a single recognition element, the probe can comprise more that the recognition elements structures claimed. Further, the reply asserts there is no motivation or suggestion of combine Jayasena with Lannigan et al. However, as noted in the 35 USC 103(a) rejection above Jayasena et al. teaches multiple beacons give an increased signal relative to singly labeled probes (p. 10 paragraph 99) and as such the ordinary artisan would have motivation to include multiple regions of object and complement regions with detectable moieties as taught by Jayasena et al. to the probe structure of Lannigan et al. The ordinary artisan would be motivated to modify the probe structure to include multiply labeled structures in order to increase signal and therefore increase the detection of the target.

10. This rejection is maintained.

Claims 6, 59, 61, and 229 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lannigan et al. (US Patent 6399302 June 4, 2002) in view of Tyagi et al. (US Patent 5925517 July 20, 1999).

Tyagi et al. was cited on the IDS 4/19/2004

Lannigan et al. teaches the structure of the independent claims 1 and 5 as discussed in the 35 USC 102 presented above.

However Lannigan et al. does not teach a probe wherein the melting temperature of said first hybridized duplex decreases by at least I°C upon binding of said receptor agent to said probe ligand.

Tyagi et al. teaches that the melting temperature of the probe is altered based upon the hybridization to the target. With regard to Claim 6, Tyagi et al. teaches an affinity probe (Figure 1 and Column 10 lines 25-40). Tyagi et al. teaches that the probe has two arms which are complementary to each other and form a hybridized duplex (Figure 1). One arm would be considered the first object and the other arm is complementary and would be considered a complement sequence (Figure 1). Tyagi et al. teaches the melting temperature of the duplex decreases by at least 10°C when hybridized (column 13 lines 1-9).

With regard to Claim 59, Tyagi et al. teaches the melting temperature of the first hybridized duplex is at least 10°C when the target is not present (column 13 lines 1-9).

With regard to Claim 61, Tyagi et al. teaches the melting temperature of the duplex decreases by at least 10°C when hybridized (e.g. when in presence of an excess of target) (column 13 lines 1-9).

With regard to Claim 229, Tyagi et al. teaches an example of a biotin labeled probe which would be considered a probe ligand (column 22 lines 15-30).

Therefore it would be prima facie obvious to one of ordinary skill in the art that the probe structure of Lannigan et al. would include the melting temperature of Tyagi et al. when hybridized to the target. It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the known melting temperature of a hybridized duplex taught by Tyagi et al. to the probes of Lannigan et al. with a predictable expectation that the probe of Lannigan et al. when hybridized to the target would have a decreased melting temperature of at least 10°C. As both the probes of Lannigan et al. and Tyagi et al. are molecular beacon type probes it would be obvious that because of the structural similarities in the hybridization structure of Lannigan et al. and Tyagi et al that the probes of Lannigan et al would also display a difference in melting temperature in the first hybridization duplex (e.g. when the objection and the complementary regions are combined) and in the second hybridization duplex (e.g. when the probe is hybridized to the target).

Response to Arguments

The reply traverses the rejection. A summary of the arguments presented in the reply is provided below with response to arguments following.

The reply asserts that the teachings of Tyagi et al. does not cure the deficiencies of Lannigan with regard to the teaching of a single recognition element (p. 16 last paragraph). The reply further asserts that there is no suggestion or teaching in Tyagi to make and use a probe taken individually or together with Lannigan (p. 17 1st paragraph).

This argument has been fully reviewed but has not been found persuasive.

As noted in the 35 USC 102 rejection and arguments presented above, the claimed probe is claimed with open claim language and as such even though there is a recitation of a single recognition element, the probe can comprise more that the recognition elements structures claimed. Further, the reply asserts there is no motivation or suggestion of combine Tyagi et al with Lannigan. However, as noted in the 35 USC 103(a) rejection above that as both the probes of Lannigan et al. and Tyagi et al. are molecular beacon type probes with similar structures that the probes of Lannigan et al. would also display a difference in melting temperature between the first hybridization duplex (e.g. closed formation) and the second hybridization duplex (e.g. open formation) based upon the hybridization to particular target sequence.

11. Claims 82-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lannigan et al. (US Patent 6399302 June 4, 2002) in view of Kolesar et al. (US Patent 6261781 July 17, 2001).

Kolesar et al. was previously cited on a PTO-892

Lannigan et al. teaches the structure of the independent claims 1 and 5.

However Lannigan et al. does not teach a probe in which the detectable label is an intercalating dye that can preferentially bind to double-stranded nucleic acids.

With regard to Claim 82, Kolesar et al. teaches probes with a detectable label such as an intercalating dye (Column 7, lines 35-50).

Therefore the combination of Lannigan et al. with Kolesar et al teaches a probe with an intercalating dye. With regard to Claim 83, Lannigan et al. teaches a probe

which comprises a first and second molecule comprising a first object and complement sequence (column 6 lines 60-65).

With regard to Claims 84 and 89, Lannigan et al. teaches that the first object or first complement is immobilized to a support (column 2 lines 40-45).

With regard to claim 85, Lannigan et al teaches that the first object and complement are linked to the reorganization element; this element is a nucleic acid structure which is covalently linked, in the first hybridization duplex, this structure would be a loop moiety (column 6 lines 50-65).

With regard to Claim 86, Lannigan et al. teaches that this reorganization element is between the object and the complement sequences and as such connect to the 3' terminus of the object and the 5' terminus of the complement (column 6 lines 50-65).

With regard to Claim 87, Lannigan et al. teaches that A and B (recognition elements) can range from 10 to about 100 bases (column 6 lines 58-60).

With regard to Claim 88, Lannigan et al. teaches a structure that comprising in the 5' to 3' direction a first object, a loop moiety (A and B), and a complement sequence (column 6 lines 58-60).

Therefore it would be prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the probe of Lannigan et al. to have an intercalator detectable label as taught by Kolesar et al. with a reasonable expectation of success. The ordinary artisan would be motivated to modify the probe of Lannigan et al. to have an intercalator detectable label as taught by Kolesar et al. because Kolesar et al. teaches that using an intercalating dye in a duplex hybrid dramatically increases

the stability of the hybrid (Column 7, lines 35-50). Therefore the ordinary artisan would be motivated to label with intercalating dye to increase stability and there increased detection of target: probe hybrids.

Response to Arguments

The reply traverses the rejection. A summary of the arguments presented in the reply is provided below with response to arguments following.

The reply acknowledges that the recitation of the Tyagi et al. patent in the obviousness rejection was an inadvertent oversight and the response to arguments is without reference to the Tyagi patent (p. 14 3rd paragraph).

The reply asserts that the teachings of Kolesar et al. do not cure the deficiencies of Lannigan with regard to the teaching of a single recognition element (p. 17 3rd paragraph). The reply further asserts that there is no suggestion or teaching in Kolesar to make and use a probe taken individually or together with Lannigan (p. 17 3rd paragraph).

This argument has been fully reviewed but has not been found persuasive.

It is noted that recitation of the Tyagi reference on p 21 2nd paragraph was a typographical error and it should have been Lannigan et al. However, it is noted that the response to arguments is based upon Lannigan in view of Kolesar. Further, the rejection and all the recitations cited in the rejection are listed as “Lannigan et al. teaches”.

As noted in the 35 USC 102 rejection and arguments presented above, the claimed probe is claimed with open claim language and as such even though there is a

recitation of a single recognition element, the probe can comprise more that the recognition elements structures claimed. Further, the reply asserts there is no motivation or suggestion of combine Kolesar et al. with Lannigan. However, as noted in the 35 USC 103(a) rejection above it would be obvious to one of ordinary skill in the art at the time of filing to modify the probe of Lannigan with the intercalator detectable label as taught by Kolesar because Kolesar et al. teaches using intercalating dye in a duplex hybrid dramatically increases the stability of the hybrid (column 7 lines 35-50). As such the modification of the probe of Lannigan et al. to include an intercalator detectable would allow an increased stability of the hybrid which is formed.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KATHERINE SALMON whose telephone number is (571)272-3316. The examiner can normally be reached on Monday - Friday 9AM-530PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Katherine Salmon/
Examiner, Art Unit 1634